

OAR	SD,cm				Mean SD, cm			
	Pat. 1	Pat. 2	Pat. 3	Pat. 4	Pat. 1	Pat. 2	Pat. 3	Pat. 4
Rectum	0.34	0.48	0.46	0.37	-0.06	-0.06	-0.06	-0.04
Sigmoid	1.39	0.96	0.72	0.66	0.44	0.22	0.18	0.17
Anus	0.81	0.99	0.54	0.68	-0.07	-0.13	-0.09	-0.09
Femoral heads	1.66	1.49	1.45	1.47	-0.44	-0.4	-0.41	0.43
Penile bulb	0.43	0.33	0.27	0.39	-0.02	-0.04	-0.03	-0.11

A SD of 0.5-1 cm was measured for the anus with the largest discrepancies for its proximal part. A good correlation between delineations was observed for the rectum with a SD of 0.3-0.5 cm with the largest discrepancy for its distal part. The sigmoid had a SD of 0.6-1.4 cm between observers with the largest discrepancies for its distal part. A SD of 1.4-1.7 cm was observed between delineation of the femoral heads with largest discrepancies for their distal parts. A small SD of 0.3-0.4 cm was obtained for the penile bulb.

**Conclusions:** Given SD < 0.5 cm for the rectum and penile bulb, the suggested guidelines were easy to follow and found sufficient in delineation of these OARs. Larger SD in delineation of the anus, sigmoid and femoral heads appeared to result from incomplete guidelines for those OARs. Stricter guidelines with better definition of OAR anatomical borders-particularly the proximal borders of the anus and distal borders of sigmoid and femoral heads- are needed.

## PROFFERED PAPERS: PREVENT 3: CARDIAC TOXICITY

### OC-0258

#### Dosimetric modeling of cardiac toxicity in patients with esophageal cancer receiving radiotherapy

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**Purpose/Objective:** New treatments are being introduced in the treatment of locally advanced esophageal cancer. Some, such as trastuzumab, can potentially increase cardiotoxicity. The purpose of this study was to model cardiac toxicity using an empirical normal tissue complication probability (NTCP) model in patients with esophageal cancer treated in part with radiotherapy.

**Materials and Methods:** Cardiotoxicity as measured by Common Toxicity Criteria Adverse Events (CTCAE) v3.0 and Radiation Therapy Oncology Group (RTOG) toxicity grading scale was identified by retrospective chart review. The probability of cardiac toxicity as a function of absorbed dose in a partial volume was modeled by the method of Lyman, by converting the dose volume histograms into an equivalent fractional volume receiving the maximum dose in the DVH, using the effective volume method of Kutcher and Burman. The parameters in this model (D50, slope  $m$  and volume exponent  $n$ ) were determined by maximum likelihood estimation. Doses prescribed in fractional doses other than 1.8 Gy were converted to equivalent dose in 1.8 Gy fractions assuming an  $\alpha/\beta$  ratio of 1.4 Gy, determined from this data set by intercomparing combinations of total dose and dose per fraction giving similar levels of toxicity.

**Results:** From 6/02 to 4/12, 150 patients (113 male and 37 female) with locally advanced esophageal cancer undergoing pre-operative or definitive CRT at 2 NCI Comprehensive Cancer Centers form the basis of this analysis. The mean radiotherapy dose was 4912 (range:3000-5940) cGy. Chemotherapy was at the discretion of the treating medical oncologist. Thirty-four (23%) developed a cardiac toxicity with 10 being symptomatic ( $\geq$  grade 3 toxicity). The mean time to any toxicity was 8 (range:1-29) months. Cardiac toxicity types were Pericardial effusion-27; Heart failure- 2, Atrial Fibrillation-1, Cardiomegaly-1, Ischemia-1, MI-1, Sick sinus syndrome-1. The maximum likelihood fit of the Lyman model parameters to patients with cardiac symptoms were  $n = 0.4$   $m = 0.34$ ,  $TD50=54.2$  Gy for men and  $TD50=41.8$  Gy for women,  $p=0.027$ .

**Conclusions:** These results are comparable to earlier reports. What is not known, however, is the use of a single toxicity endpoint rather than combined endpoints. The pathophysiologic etiology of pericardial

effusion most likely is not the same as heart failure, one being an effect on the pericardium while the other an effect on the cardiac myocytes. Further work is needed to clarify the dose resulting in toxicity to each cardiac structure necessary to result in cardiotoxicity and why we see a difference between men and women.

### OC-0259

#### Radiotherapy/chemotherapy-related cardiovascular disease in breast cancer patients: a population-based study

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**Purpose/Objective:** Several studies have shown that breast cancer treatment may increase the risk of cardiovascular disease after ten or more years. However, most reports are based on older treatment regimens. It is not known whether more contemporary radiation techniques are associated with excess cardiovascular disease. In addition, it is not clear whether current chemotherapeutic regimens, especially regimens containing anthracyclines, increase the risk of cardiovascular disease in breast cancer survivors.

The aim of this study is to assess the effect of radiotherapy and chemotherapy for breast cancer on cardiovascular morbidity and mortality.

**Materials and Methods:** We have constructed a large population-based cohort of patients diagnosed with invasive breast cancer between 1989 and 2004 ( $n=93,630$ ). Information on patient characteristics, primary and secondary malignancies, and basic treatment information (e.g. type of surgery, radiotherapy yes/no, chemotherapy yes/no) were provided by the Netherlands Cancer Registry. Detailed treatment information was collected through electronic files from radiotherapy institutes, trials, and regional studies. Date and cause of death were acquired through linkage with the Central Bureau for Genealogy and Statistics Netherlands, respectively, until January 2010. Data on cardiovascular morbidity were acquired through linkage with two registries: the Hospital Discharge Registry (LMR) and the Cardiac Interventions Registry (BHN). **Results:** Of the initial 93,630 patients, 69,123 survived at least five years after breast cancer diagnosis. The median follow-up of five-year survivors was 9.7 years (range 5-21 years).

We distinguished four mutually exclusive treatment categories: surgery only (33%), radiotherapy with or without surgery (46%), radiotherapy and chemotherapy with or without surgery (15%), and chemotherapy with or without surgery (6%). 52% of the patients treated with radiotherapy were irradiated for left-sided breast cancer. Due to the anatomical position of the heart, the radiation-dose to the heart is higher during left-sided radiotherapy than during right-sided radiotherapy.

At the PREVENT meeting, results will be presented on the evaluation of mortality rates in comparison with the general population. Secondly, we will present comparisons of cardiovascular mortality rates and incidence of different cardiovascular diseases between the above stated treatment categories, and more specifically by type of chemotherapeutic, radiation field, and laterality.

**Conclusions:** Based on our results, conclusions will be drawn with respect to the effects of modern radiotherapy regimens and specific chemotherapeutics for breast cancer.

### OC-0260

#### Effects of a tocotrienol-enriched formulation in a rat model of local heart irradiation

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**Purpose/Objective:** Radiation-induced heart disease (RIHD) is a long-term side effect of radiotherapy of intrathoracic and chest wall tumors when radiation fields encompass all or part of the heart. Tocotrienols are forms of vitamin E with potent radioprotective properties. This study investigates the effects of pre-treatment and